INST. FÖR CELLFORSKNING OCH GENETIK
MEDICINSKA NOBELINSTITUTET
KAROLINSKA INSTITUTET
STOCKHOLM 60
Telefon 23 54 80

INST. FOR CELL RESEARCH AND GENETICS
KAROLINSKA INSTITUTET
STOCKHOLM 60

October 9,1954

Professor Joshua Lederberg
University of Wisconsin
Madison 6,Wisc.
U.S.A.

My dear Lederberg,

many thanks for your letter of October 4. With regard to the effect of mitochondria from non-specific sources,this was a mistake on my part. I was simply mixing up available evidence on mitotic stimulation with that on "resuscitation". I know of no experiments on resuscitation with mitochondria from non specific sources. Sorry!

Many thanks for your stimulating comments on our "transduction" trials. Indeed,we should evaluate our detection methods with reconstruction experiments and have already started one since your letter came. Also,we have obtained some of Law's drug-resistant lines and intend to use them for transduction experiments as soon as have got their growth curves straight.

With regard to the experiments of Stasney et al., I should not attribute too much significance to the fact that no cells were detected. The work on single-cell clones has shown that one cell may be quite sufficient to produce tumors within quite short periods of time. Even if quite a number of tumor cells were contained in the "chromatin" fraction,the smear method used by Stasney et al, and,repeating their work,by myself,is grossly unadequate to detect them as long as their total mass remains a small fraction of the total material. The fact that Stasney et al. could produce a similar number of tumors with similar latency periods only by injecting cells of the order of a hundred thousand in control experiments does not prove anything,as the control cells were suspended in damaging saline media while the presumptive undetected cells were embedded into large and probably protective masses of chromatin. I feel that the subcutaneous inoculation of the material is a kind of DNAse experiment in vivo; tissue fluid and serum is so rich in DNAse that polymerized DNA could not maintain itself unchanged for any considerable period of time, would you not agree on this?

As to possible recombination between intact cells in mixed culture,we have been thinking of the following experiment: We have two lymphomas,very similar morphologically and in growth characteristics,but specific for two different inbred strains. One of them has an amethopterin resistant subline while the other is sensitive. We thought of mixing these two in equal proportion and letting them grow one generation in the F_1 hybrid. After this they would be separated by reinoculation into the original parent strain,and the originally sensitive line would be tested for resistancy. Do you think that this is a reasonable experiment?

In this experiment, again, reconstruction methods could be used to evaluate the sensitivity of the detection procedure.

Thank you very much again for all your valuable comments,

yours sincerely,

Horst Klein